

JC02 Rec'd PCT/PTO 24 MAY 2002

I hereby certify that this correspondence is being deposited with the United States Postal Service on the date set forth below as First Class Mail in an envelope addressed to: Commissioner for Patents, P O Box 2327, Arlington, VA 22202.

Date of Signature and Deposit: May 21, 2002

Zhibin Ren

Zhibin Ren

PATENT



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Richard J. Roman  
David R. Harder  
Noriyuki Miyata  
Masakazu Sato  
Kazuya Kameo  
Shigeru Okuyama

Date: May 21, 2002

Serial No.: 09/937,946

Group Art Unit:

Filed: 10/02/2001

Examiner:

Title: USE OF 20-HETE SYNTHESIZING ENZYME  
INHIBITORS AS THERAPY FOR CEREBRAL  
VASCULAR DISEASE

File No.: 650053.91533

#### INFORMATION DISCLOSURE STATEMENT

Commissioner For Patents  
Box Non-Fee  
P O Box 2327  
Arlington, VA 22202

Dear Sir:

Enclosed is a completed Form PTO-1449 listing documents that the applicants in the above-identified application wish to bring to the attention of the Examiner for consideration in connection with the examination on the merits of this application.

No fee is believed due in connection with this submission. However, if a fee is due, please charge the fee to Deposit Account No. 17-0055.

Respectfully submitted,

Zhibin Ren

Zhibin Ren

Reg. No. 47,897

Attorney for Applicants

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P O Box 2113

Madison, WI 53701-2113

TEL 608/251-5000

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Form PTO-1449  
(Rev. 2-88)U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICE

ATTY. DOCKET NO.

SERIAL NO.

650057533

09/937,946

APPLICANT(S):

Roman/Harder/Miyata/Sato/Dameo/Okuyama

FILING DATE:

10/02/2001

GROUP

INFORMATION DISCLOSURE STATEMENT  
BY APPLICANT

(Use several sheets if necessary)

MAY 24 2002

## U.S. PATENT DOCUMENTS

EXAMINER'S INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO
	WO 01/32164	10.05.2001	Japan				

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		Alonso-Galicia, M. et al., "Inhibition of 20-HETE Production Contributes to the Vascular Responses to Nitric Oxide," <u>Hypertension</u> 29:320-325 (1997)
		Alonso-Galicia, M., et al., "Contribution of 20-HETE to Vasodilator Actions of Nitric Oxide in the Cerebral Microcirculation," <u>Stroke</u> 30:2727-2734 (1999)
		Alonso-Galicia, M., et al., "20-HETE agonists and antagonists in the renal circulation," <u>Am. J. Physiol.</u> 277:F790-F796 (1999)
		Amet, Y., et al., "Cytochrome P450 4A and 2E1 Expression in Human Kidney Microsomes," <u>Biochemical Pharmacology</u> 53:765-771 (1997)
		Amet, Y., et al., "Noninvolvement of CYP2E1 in the (ω-1)-hydroxylation of Fatty Acids in Rat Kidney Microsomes," <u>Biochemical Pharmacology</u> 54:947-952 (1997)
		Amet, Y., et al., "P-450-Dependent Metabolism of Lauric Acid in Alcoholic Liver Disease: Comparison Between Rat Liver and Kidney Microsomes," <u>Alcoholism: Clinical and Experimental Research</u> 22:455-462 (1998)
		Bednar, M.M., et al., "16(R)-Hydroxy-5,8,11,14-eicosatetraenoic Acid, a New Arachidonate Metabolite in Human Polymorphonuclear Leukocytes," <u>Biochemical Pharmacology</u> 60:447-455 (2000)
		Christmas, P., et al., "Alternative Splicing Determines the Function of CYP4F3 by Switching Substrate Specificity," <u>Journal of Biological Chemistry</u> 276:38166-38172 (2001)
		Clozel, M. et al., "BQ-123, A Peptidic Endothelin ET <sub>A</sub> Receptor Antagonist, Prevents the Early Cerebral Vasospasm Following Subarachnoid Hemorrhage After Intracisternal But Not Intravenous Injection," <u>Life Sciences</u> 52:825-834 (1993)
		Croft, K., et al., "Angiotensin II releases 20-HETE from rat renal microvessels," <u>Am. J. Physiol. Renal Physiol.</u> 279:F544-F551 (2000)
		Dahly, A.J., et al., "Chronic Anti-TGF-β Therapy Improves Blood Pressure and Renal Function in Dahl S Rats," <u>FASEB J.</u> 14:A133 (2000)
		Dahly, A.J., et al. "Chronic Anti-TGF-β Ab Therapy Reduces Proteinuria and Renal Injury in Hypertensive Rats," <u>American Society of Nephrology Renal Week</u> 11:332A (2000)
		Gebremedhin, D., et al., "Cat cerebral arterial smooth muscle cells express cytochrome P450 4A2 enzyme and produce the vasoconstrictor 20-HETE which enhances L-type Ca <sup>2+</sup> current," <u>Journal of Physiology</u> 507.3:771-781 (1998)

EXAMINER

DATE CONSIDERED

\* EXAMINER: Initial if a citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. QBMA0332105

Form PTO-1449

(Rev. 2-88)

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICE

ATTY. DOCKET NO.

65005 1533

SERIAL NO.

09/937,946

**INFORMATION DISCLOSURE STATEMENT  
BY APPLICANT**

(Use several sheets if necessary)

APPLICANT(S)  
Roman/Harder/Miyata/Sato/Dameo/Okuyama

FILING DATE:

10/02/2001

GROUP

**U.S. PATENT DOCUMENTS**

* EXAMINER'S INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

**FOREIGN PATENT DOCUMENTS**

FOREIGN PATENT DOCUMENTS								
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

		Gebremedhin, D., et al., "Production of 20-HETE and Its Role in Autoregulation of Cerebral Blood Flow," <u>Circulation Research</u> 87:60-65 (2000)
		Harder, D.R., et al., "Formation and action of a P-450 4A metabolite of arachidonic acid in cat cerebral microvessels," <u>American Physiological Society</u> 266:H2098-H2107 (1994)
		Juvela S., "Plasma endothelin concentrations after aneurysmal subarchnoid hemorrhage," <u>J. Neurosurg.</u> 92:390-400 (2000)
		Oyekan, A., et al., "Renal oxygenases: differential contribution to vasoconstriction induced by ET-1 and ANG II," <u>American Physiological Society</u> 273:R293-R300 (1997)
		Powell, P.K., et al., "Metabolism of Arachidonic Acid to 20-Hydroxy-5,8,11,14-eicosatetraenoic Acid by P450 Enzymes in Human Liver: Involvement of CYP4F2 and CYP4A11," <u>Journal of Pharmacology and Experimental Therapeutics</u> 285:1327-1336 (1998)
		Rosolowsky, M., "Metabolism of arachidonic acid by canine polymorphonuclear leukocytes synthesis of lipoxygenase and omega-oxidized metabolites," <u>Biochimica et Biophysica Acta</u> 1300:143-150 (1996)
		Seifert, V., et al., "Endothelin concentrations in patients with aneurysmal subarachnoid hemorrhage," <u>J. Neurosurg.</u> 82:55-62 (1995)
		Wang, M., et al., "Contribution of cytochrome P-450 4A1 and 4A2 to vascular 20-hydroxyeicosatetraenoic acid synthesis in rat kidneys," <u>American Physiological Society</u> 276L:F246-F253 (1999)
		Wang, M., et al., "Cytochrome P450-Derived Arachidonic Acid Metabolism in the Rat Kidney: Characterization of Selective Inhibitors," <u>The Journal of Pharmacology and Experimental Therapeutics</u> 284:966-973 (1998)
		Zou, A., et al., "Effects of 17-Octadecynoic Acid, a Suicide-Substrate Inhibitor of Cytochrome P450 Fatty Acid $\omega$ -Hydroxylase, on Renal Function in Rats," <u>The Journal of Pharmacology and Experimental Therapeutics</u> 268:474-481 (1994)

EXAMINER

DATE CONSIDERED

\* EXAMINER: Initial if a citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. QBMA0\332105

**FEE TRANSMITTAL  
FOR FY 2002**

MAY 24 2002

Patent fees are subject to annual revision.

TOTAL AMOUNT OF PAYMENT

\$

**Complete if Known**

Application Number	09/937,946
Filing Date	10/02/2001
First Named Inventor	Richard J. Roman
Group Art Unit	
Examiner Name	
Attorney Docket Number	650053.91533

**METHOD OF PAYMENT (check one)**1. ☒ The Commissioner is hereby authorized to charge indicated fees and credit any over payments to:

Deposit Account Number 17-0055

Deposit Account Name Quarles &amp; Brady LLP

☒ Charge Any Additional Fee Required Under 37 CFR 1.16 and 1.17☐ Applicant claims small entity status See 37 CFR 1.272. ☐ Payment Enclosed:☐ Check ☐ Credit Card ☐ Money Order ☐ Other**FEE CALCULATION****1. BASIC FILING FEE**

Large Entity Fee Code	Large Entity Fee (\$)	Small Entity Fee Code	Small Entity Fee (\$)	Fee Description	Fee Paid
101	740	201	370	Utility filing fee	
106	330	206	165	Design filing fee	
107	510	207	255	Plant filing fee	
108	740	208	370	Reissue filing fee	
114	160	214	80	Provisional filing fee	

SUBTOTAL (1) (\$).00

**2. CLAIMS**

Total Claims	Extra	Fee from below	Fee Paid
Independent	-20**=	X	
Multiple Dependent Claims	-3**=	X	

\*\* or number previously paid, if greater, For reissues see below

Large Entity Fee Code	Large Entity Fee (\$)	Small Entity Fee Code	Small Entity Fee (\$)	Fee Description
103	18	203	9	Claims in excess of 20
102	84	202	42	Independent claims in excess of 3
104	280	204	140	Multiple dependent claim
109	84	209	42	**Reissue independent claims over original patent
110	18	210	9	**Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) (\$).00

**FEE CALCULATION (continued)****3. ADDITIONAL FEES**


Large Entity Fee Code	Large Entity Fee (\$)	Small Entity Fee Code	Small Entity Fee (\$)	Fee Description	Fee Paid
105	130	205	65	Surcharge - late filing fee or oath	
127	50	227	25	Surcharge - late provisional filing fee or cover sheet	
139	130	139	130	Non-English specification	
147	2,520	147	2,520	For filing a request for reexamination	
112	920	112	920	Requesting publication of SIR prior to Examiner action	
113	1,840	113	1,840	Requesting publication of SIR after Examiner action	
115	110	215	55	Extension for reply within first month	
116	400	216	200	Extension for reply within second month	
117	920	217	460	Extension for reply within third month	
118	1,440	218	720	Extension for reply within fourth month	
128	1,960	228	980	Extension for reply within fifth month	
119	320	219	160	Notice of Appeal	
120	320	220	160	Filing a brief in support of an appeal	
121	280	221	140	Request for oral hearing	
138	1,510	138	1,510	Petition to institute a public use proceeding	
140	110	240	55	Petition to revive unavoidably abandoned application	
141	1,280	241	640	Petition to revive unintentionally abandoned application	
142	1,280	242	640	Utility issue fee (or reissue)	
143	460	243	230	Design issue fee	
144	620	244	310	Plant issue fee	
122	130	122	130	Petitions to the Commissioner	
123	50	123	50	Petitions related to provisional applications	
126	180	126	180	Submission of Information Disclosure Stmt	
581	40	581	40	Recording each patent assignment per property (times number of properties)	
146	740	246	370	Filing a submission after final rejection (37 CFR 1.129(a))	
146	740	246	370	For each additional invention to be examined (37 CFR 1.129(b))	
179	740	270	370	Request for Continued Examination (RCE)	
169	900	169	900	Request for expedited examination of a design application	

Other fee (specify) \_\_\_\_\_

\* Reduced by Basic Filing Fee Paid

SUBTOTAL (3) (\$).00

**SUBMITTED BY****Complete (if applicable)**

Typed or Printed Name	Zhibin Ren	Registration No. (Attorney/Agent)	47,897	Telephone	608/251-5000
Signature				Date	May 21, 2002